REMARKS

Claims 1 and 18-44 are now pending in the application, claims 2-17 having been canceled by the present amendment and claims 18-44 having been added. **Claim 1** has been amended to specify that the therapeutic agents claimed prevent interaction between a first protein and a second protein. This amendment is supported by the specification at, for example, page 3, lines 4-6.

New **claim 18** is supported throughout the specification (see, *e.g.*, the first full paragraph on page 5). New **claims 19-22, 24-27, and 39** are supported by the specification at, for example, page 5, lines 3-7 and 19-28 (*see also* original claim 6). New **claim 23** is supported by original claim 7 (*see also*, the specification at, for example, page 5, lines 27-28). New **claim 28** is supported by original claim 9, and new **claim 29** is supported by original claim 9. New **claims 30-32** are supported by, for example, Figures 1 and 2, by Example 1, and by the specification at page 5, lines 27-28. New **claim 33** is supported by original claim 10. New **claim 34** is supported by the first full paragraph on page 5 and by, for example, page 6, lines 8-9). New **claims 35 and 36** are supported by the specification at, for example, page 3, lines 13-16. New **claim 37** is supported by the specification at, for example, page 4, lines 23-28. New **claim 38** is supported by the specification at, for example, page 10, line 28 through page 11, line 3. New **claims 40-43** are supported by the specification at, for example, page 3, lines 4-6 and page 5, lines 11-17. New **claim 44** is supported by, for example, original claim 11. No new matter has been added.

Priority Claim

The Examiner notes that an application, where appropriate, must contain a specific reference to the prior application(s) in the first sentence of the specification. (Office action at page 2).

Applicants respectfully submit that the present application contains such a reference. The Examiner's attention is directed to the first page of the specification, at lines 3-5. Should the

Examiner consider there to be an error in the priority claim made, the favor of a telephone call to the undersigned is respectfully requested.

Objections to the Specification

The Examiner states, "[t]he title of the invention is not descriptive" (Office action at page 2).

The present title of the application is "Inhibition of protein-protein interaction." As Applicants' claims cover therapeutic agents that prevent interaction between a first protein and a second protein, Applicants fail to understand how the present title fails to indicate the invention. Applicants are willing to amend the title, should the Examiner maintain this objection. However, further guidance as to the nature of a satisfactory amendment would be appreciated.

The Examiner also notes that the specification contains underlined text, and suggests removing the underline (Office action at page 2).

Upon a review of the specification, the only text that appears to be underlined is the text within certain headings and the volume numbers in referenced journal articles. As Applicants presently have no intention of amending this text, and as it is standard practice to set out the volume of a journal by underlining, Applicants would prefer not to remove the present underlining. Moreover, Applicants' representative has added text to underlined matter in other applications by way of a double underline. Should the Examiner continue to believe that the presently underlined text may create confusion, the favor of a telephone call to the undersigned is respectfully requested.

35 U.S.C. § 102(b)

Claims 1, 5, 6, 8, 9, and 10 are rejected as being anticipated by Peterson *et al.* (*Science* 248:1625-1630, 1990; herein, "Peterson"). As the Examiner's argument is brief, we reproduce it below in its entirety for the sake of completeness and easy reference (Office action at page 4).

Peterson et al teach the cloning of human TATA binding factor comprising SEQ ID NO:11 (amino acid 270-337). TATA binding protein binds coactivator transcription factors that contain multiple consecutive glutamine residues. TATA binding protein comprises alpha-helical and beta-sheet structural motifs (current application claims 1, 5, 6, 8, 9, and 10).

In view of the present amendment to claim 1, from which all the presently pending claims depend or ultimately depend, Applicants request reconsideration of this ground for rejection. Claim 1 covers a therapeutic agent that prevents interaction between a first protein and a second protein. The naturally occurring TATA binding protein disclosed by Peterson (TFIID) cannot meet this limitation. TFIID, as demonstrated by Paterson, "binds specifically to a TATA box and promotes basal transcription" (Abstract). Further, Paterson teaches, "TFIID forms a stable complex on a TATA box either alone or in combination with either of the general transcription factors, TFIIa or TFIIB" (Abstract). Thus, TFIID interacts with DNA sequences and transcription factors within cells to *facilitate* their interaction in a way that promotes gene expression; TFIID does not, prevent interaction between proteins. Accordingly, Paterson cannot anticipate the therapeutic agents now claimed.

35 U.S.C. § 103

Claims 1-11 are rejected as being obvious over Housman *et al.* (U.S. Patent 6,420,122; herein, "Housman") in view of Preisinger *et al.* (*Phil. R. Soc. Lond. B* 354:1029-1034, 1999). The Examiner states that Housman discloses "a polypeptide with extended polyglutamine regions" including a polypeptide that contains "the first 17 amino acids [*sic.*] of the huntingtin protein fused to 25 glutamine residues fused with either a 28 amino acid c-myc tag or with a 230 amino acid enhanced fluorescent protein tag" (Office action at pages 4-5, citing Housman at column 5, line 64 through column 13, line 10). The Examiner then characterizes Preisinger as disclosed an "interaction of extended polyglutamine proteins with cellular non-extended polyglutamine containing proteins, as a mechanism for the pathogenesis in polyglutamine neurodegenerative disorders" (Office action at page 5, citing Preisinger at page 1033). The Examiner then concludes that one of ordinary skill in the art "would have been motivated to

identify competitive peptides that interact with extended polyglutamine containing peptides, which could be of therapeutic benefit in polyglutamine neurodegenerative disorders" (Office action at page 5). The Examiner's final remark is that "it would have been obvious ... to have a therapeutic peptide that binds polyglutamine proteins with a spacer to physically separate and suppress the aggregation of cellular polyglutamine containing proteins" (Office action at page 5, *citing only to the current application, claims 1-11*).

This ground for rejection is respectfully traversed. For a *prima facie* case of obviousness, the prior art must meet three criteria. The prior art must teach or suggest all of the limitations of the invention now claimed; there must be some motivation to modify the prior art to arrive at the present invention; and there must be a reasonable expectation of success.

In the present case, there is no suggestion whatsoever that one should make a therapeutic agent having three domains, the third of which separates a first domain from a second domain to such an extent that proteins bound to the first and second domains cannot interact as they otherwise would. Housman focuses on "methods of identifying compounds that disrupt [protein-protein] aggregation" (Abstract). Polypeptides with extended polyglutamine (polyQ) regions are certainly used in Housman's screening methods, but there is no suggestion that those polypeptides should be used – or modified and used – as therapeutic agents themselves. Housman's polyglutamine-containing proteins are distinct from the therapeutic agents now claimed. In particular, Housman is silent with respect to the required third domain, as is Preisinger. Preisinger is a fundamental research article on the mechanism by which polyQ-containing polypeptides aggregate. Preisinger discovered that, when "normal length" polyQ polypeptides were transfected into cells, they did not aggregate. However, and "[r]emarkably", these normal length polypeptides *did* aggregate when co-transfected with polypeptides containing extended polyQ tracts (Abstract). Nothing in Preisinger's recruitment and sequestration study suggests, however, the tri-domain agent now claimed. Simply recognizing that it would be beneficial to inhibit aggregation is not enough. By way of analogy to the field of cancer treatment: fundamental studies of tumor growth quickly led to the realization that it would be beneficial to inhibit cellular proliferation, but that is not enough to render obvious a

specific therapeutic agent, even if that agent is a relatively simple one, and even if a part of that agent may have been used in research studies or screening methods. For obviousness, *all* of the limitations of the present claims, *and* the motivation to modify the teaching of the prior art, must be found *in the prior art* or taken from generally available knowledge, *not* Applicants' specification. Even when combined, Housman and Preisinger do not teach therapeutic agents having the first, second, and third domains required by Applicants' claim 1 (and by the claims that depend therefrom), nor is there motivation *in those disclosures* to modify the polyQ-containing proteins Housman and Preisinger used to arrive at the therapeutic agents Applicants now claim.

Moreover, as neither Housman nor Preisinger worked with any agents that were configured as the therapeutic agents now claimed, neither Housman nor Preisinger can supply the requisite expectation for success. While physical separation *may* have been "obvious to try," Applicants see nothing in Housman and Preisinger that would provide one of ordinary skill in the art with a reasonable expectation that the therapeutic agents now claimed would succeed. Many therapies that have seemed sure bets have, instead, failed when put to the test. Thus, even if a "spacer" had been worthy of a try, the law is clear: more is required for *prima facia* obviousness. Accordingly, this ground for rejection should be withdrawn.

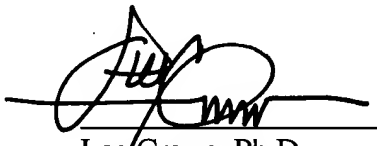
CONCLUDING REMARKS

In view of the present amendment and the remarks provided above, the present claims are considered in condition for allowance, which action is respectfully requested.

Enclosed is a check for the Petition for Extension of Time fee (one month). If there are any other charges due in this application, for any reason, of if there are any credits, please apply them to Deposit Account No. 06-1050, referencing Attorney Docket No. 01997-289001.

Respectfully submitted,

Date: May 28, 2004



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